Microbial Pathogenesis 129 (2019) 93–98

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath

Evaluation of the prevalence of *Legionella pneumophila* in Iranian clinical samples: A systematic review and meta-analysis

Azad Khaledi[a], Seyed-Alireza Esmaeili[b,c], Hossein Vazini[d], Pezhman Karami[e], Afsane Bahrami[f], Amirhossein Sahebkar[g,h,i,*]

[a] Infectious Diseases Research Center, Kashan University of Medical Sciences, Kashan, IR, Iran
[b] Immunology Research Center, Bu-Ali Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran
[c] Immunology Department, Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[d] Nursing Department Basic Sciences Faculty, Hamedan Branch, Islamic Azad University, Hamedan, Iran
[e] Department of Microbiology, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, IR, Iran
[f] Cellular and Molecular Research Center, Birjand University of Medical Sciences, Birjand, Iran
[g] Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical of Sciences, Mashhad, Iran
[h] Neurogenic Inflammation Research Center, Mashhad University of Medical of Sciences, Mashhad, Iran
[i] School of Pharmacy, Mashhad University of Medical of Sciences, Mashhad, Iran

ARTICLE INFO

Keywords:
Iran
Legionella pneumophila
Clinical samples

ABSTRACT

Background: *Legionella pneumophila* is the main cause for community-acquired pneumonia especially in hospital environments. In this systematic review and meta-analysis, we evaluated the prevalence of *L. pneumophila* in clinical samples obtained from Iranian patients.
Methods: The studies reporting *L. pneumophila* prevalence in Iranian clinical samples that were published between January 2000 and July 2016 were recruited. Comprehensive Meta-Analysis Software (version 3.3.070) was used for quantitative data analysis. Because of high heterogeneity between the studies according to the Cochrane Q and I^2 statistics, a random-effects model was used for meta-analysis.
Results: Sixteen studies encompassing 1956 subjects were included in the meta-analysis. The overall prevalence of *L. pneumophila* was 9.6% in clinical samples obtained from the Iranian patients. The age spectrum ranged from 6 months to 80 years old. Dyspnea and cough comprised the most common clinical manifestations. In the subgroup analysis, the prevalence of *L. pneumophila* was higher in studies with sample size ≤100 (12.9%) in comparison with studies with sample size > 100 (8.4%). In addition, the prevalence of *L. pneumophila* was higher in the years 2009–2016 (9.2%) compared with 2000–2008 (0.7%).
Conclusion: *L. pneumophila* is a major cause of community- and hospital-acquired pneumonia. It is of pivotal importance to implement sensitive and reliable molecular and culture-based techniques to detect and control this infection in healthcare environments.

1. Introduction

Legionella species are responsible for around 30% of hospital-acquired pneumonia (HAP) and nearly 1–3% of community-acquired pneumonia (CAP) [1]. *Legionella pneumophila* is a small Gram-negative bacillus responsible for about 2–15% of CAP and HAP respectively [1]. The bacterium is an aerobic, fastidious and motile organism with unipolar flagella and pili lacking capsule and unable to form spores [2]. The infection affects the respiratory system and is transmitted through the respiratory route [3]. This agent particularly grows in hospital environments rendering a potential for hospital-borne infection [4]. *L. pneumophila* is responsible for around 85% of Legionnaires' disease cases which can be either sporadic or epidemic [5]. The first global outbreak of hospital-acquired Legionnaires' disease was reported in 1976. The disease is mainly transmitted through micro-aspiration [6]. Although L. *pneumonia* infection has no specific clinical signs and symptoms [7], it may manifest with diarrhea, neurological problems (especially confusion), fever (usually higher than 39 °C), hyponatremia, hepatic dysfunction and hematuria [8]. Community acquired pneumonia usually presents more severe clinical manifestations compared to hospital acquired disease. This may be due to the relatively late diagnosis of the community-based disease leading to delayed therapeutic

* Corresponding author. Biotechnology Research Center, Mashhad University of Medical Sciences, Mashhad, 9177948564, Iran.
E-mail addresses: amir_saheb2000@yahoo.com, sahebkara@mums.ac.ir (A. Sahebkar).

https://doi.org/10.1016/j.micpath.2019.02.008
Received 26 January 2017; Received in revised form 4 February 2019; Accepted 4 February 2019
Available online 07 February 2019
0882-4010/

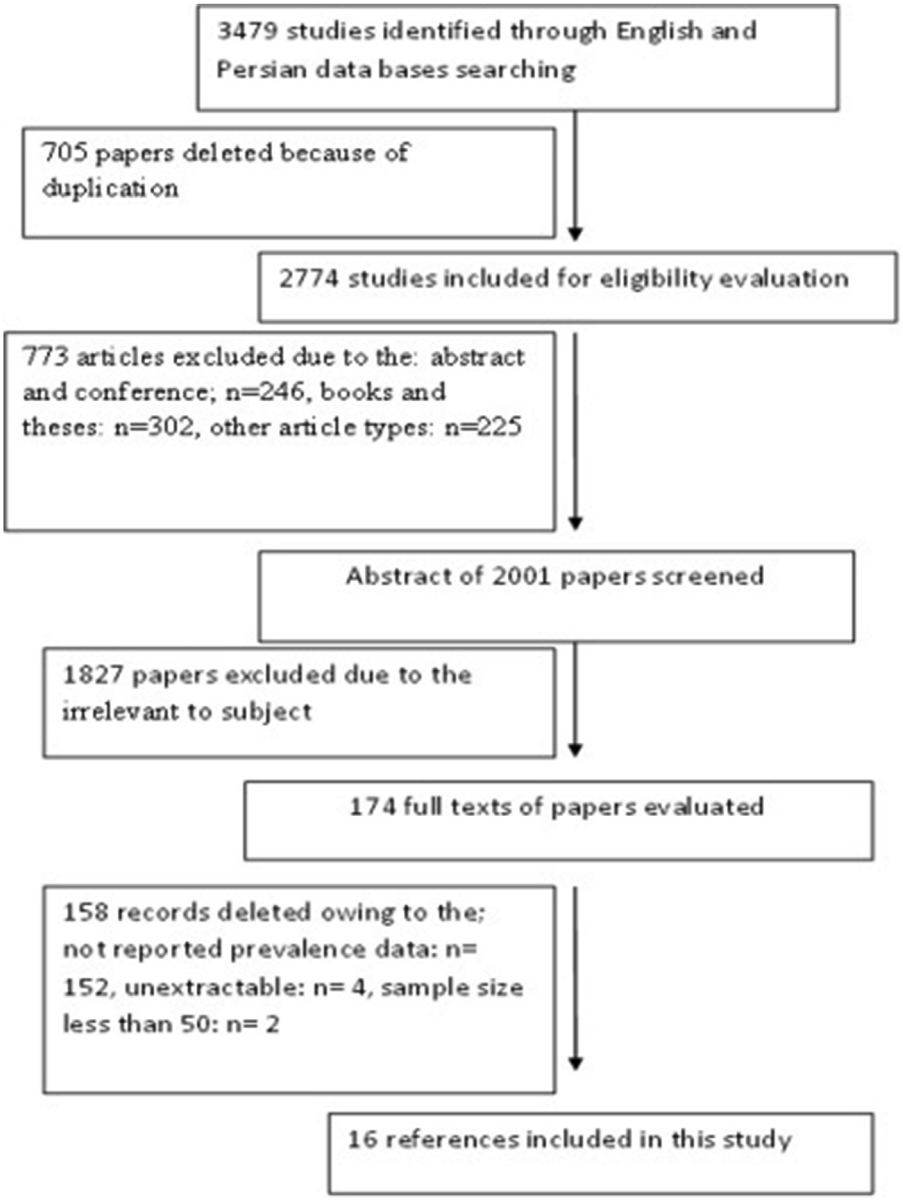

Fig. 1. Flow chart showing studies that were processed for inclusion in this study.

and antibiotic interventions. In the absence of proper antibiotic treatment, legionellosis can impose high mortality and morbidity rates (as high as 80%), particularly in immunosuppressed individuals [5] and those co-infected with other respiratory pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Mycobacterium tuberculosis*. The early diagnosis and timely initiation of the 14-day treatment course of *Legionella* infections can prevent such potential health threats. Although patients with a competent immune system appropriately respond to the treatment, patients with a compromised immune system generally fail to respond [9].

Determining the L. *pneumophila* prevalence and its contaminating sources in hospital environments are necessary to manage the infection and to evaluate the effectiveness of the coping strategies. There has been no systematic reviews on the prevalence of *L. pneumophila* in Iran. Hence, we aimed to determine the prevalence of *L. pneumophila* in clinical samples obtained from Iranian patients using a systematic review and meta-analysis of published data.

2. Methods

2.1. Search strategy

The Prisma protocol (PRISMA, http://www.prisma-statement.org) was followed in all steps of the study. The literature search was conducted in PubMed, Scopus, Web of Science, Cochrane Library, ScienceDirect, MEDLINE, Google Scholar as well as Iranian Scientific Information Database (www.sid.ir), Iranmedex (www.iranmedex.com), Magiran (www.magiran.com) and Irandoc (www.irandoc.ac.ir). The keywords included *Legionella*, Legionnaires' disease, incidence, epidemiology, hospital-acquired pneumonia, community-acquired pneumonia, prevalence, *L. pneumophila*, *Legionella* spp, *Legionella* infection, distribution and Iran. Also, the Persian equivalents of the keywords were used in Iranian databases. Those studies reporting the prevalence of L. *pneumophila* in clinical samples from Iranians patients and published from January 2000 to July 2016 were included. The research articles published in either English or Persian were recruited. The literature search was independently conducted by two professional and experienced researchers. Finally, those studies meeting the eligibility

criteria were included in the systematic review and met-analysis.

2.2. Inclusion and exclusion criteria

Original research papers (either cross-sectional, cohort or observational studies) reporting the distribution and prevalence of *Legionella* in Iranian populations published from January 2000 to July 2016 were included in this study. The review articles (either narrative or meta-analysis and systematic reviews), letters to the editors, case reports, congress papers, meeting abstracts and brief reports, articles presented in languages other than English or Persian, as well as animal studies and those conducted on environmental samples were excluded. Furthermore, duplicate publications, unpublished studies and studies with incomplete data and unclear methods, as well as studies with sample sizes less than 50 were also excluded from the study.

2.3. Data extraction

The name of the first author, publication year, location of the study, patients' age, and the prevalence of Legionellosis were recorded using a researcher-designed data checklist. The extracted data was finally verified by the study supervisor.

2.4. Statistical analysis

The Comprehensive Meta-Analysis Software (Version 3.3.070) was used for data analysis. The prevalence of *L. pneumophila* was reported by 95% confidence intervals (CIs). Because of the heterogeneity between the studies as determined by the Cochrane Q and I^2 tests, a random-effects model was used for meta-analysis. The Egger's regression test and funnel plot were used to assess the presence of any publication bias considering a $P < 0.05$ as the statistical significance threshold. In addition, the Egger's linear Regression Test was used to assess the likelihood of missing the studies on funnel-plot asymmetry.

3. Results

3.1. Study characteristics

As shown in Fig. 1, a total of 3479 studies were identified after the primary search in English and Persian databases. Out of these, 174 full texts were evaluated from which 16 studies were considered eligible to be included in the meta-analysis. All of the eligible studies were conducted on clinical samples and in different geographical areas of Iran; most of them (n = 9) conducted in Tehran city. Phenotypic as well as molecular and biochemical detection techniques which were used in the studies included morphology and smear microscopy, BCYE-a medium culture, PCR-based methods (Nested PCR, real-time PCR), DFA, ELISA and Latex agglutination. PCR-based techniques were the most commonly used molecular method. The clinical samples included BAL, urine, sputum as well as respiratory and lung secretions (see Fig. 2 and Fig. 3).

According to the meta-analysis, the prevalence of *Legionella* varied from 0.4% to 22.1% (Table 1 and Fig. 1). The largest sample size was related to the study by Fard et al. and the smallest belonged to the studies carried out by Mirkalantari et al. and Hosseini Dust et al. Totally, 1956 clinical samples were analyzed. The patients' age spectrum widely varied from 6 months to 80 years old encompassing neonates, children, adolescents, young adults, and elderly. Dyspnea and cough comprised the most common clinical manifestations in the patients. Other clinical presentations included Legionnaires' disease, COPD, asthma, respiratory infections, pneumonia, HAP and CAP.

3.2. Overall effects

As there was a significant heterogeneity between the sixteen included studies ($Q^2 = 63.4$, $I^2 = 76.3$, $t = 41$, $p = 0.000$), a random-effects model was used to estimate the combined prevalence of *L. pneumophila*. Overall, the prevalence of *L. pneumophila* in Iranian clinical samples was estimated to be 9.6% (95% Cl: 8.2, 11.1). The funnel plot test and the Egger's test ($p = 0.00$) indicated publication bias in the evaluated studies ($p = 0.00$).

3.3. L. pneumophila prevalence in subgroup analyses

Subgroups analysis showed that the prevalence of *L. pneumophila* in clinical samples obtained from the Iranian patients was higher in studies with sample siz e ≤ 100 in comparison with studies with sample size > 100 (12.9%, 95% CI: 9.9–16.7 *vs.* 8.4%, 95% CI: 7.0–10.1 (respectively. Also, subgroup analysis based on the study locations showed that the highest prevalence of *L. pneumophila* was observed in Ahvaz (17.4%, 95% CI: 11.6–25.2) and Shahrekord (12.0%, 95% CI: 8.5–16.6) cities. Subgroup analysis regarding the time of the studies revealed that the prevalence of *L. pneumophila* was higher in the years 2009–2016 (9.2%, 95% CI: 7.7–11.0) compared with the 2000–2008 (0.7%, 95% CI: 8.0–14.3) period (Table 2).

4. Discussion

Our aim was to assess the prevalence of *L. pneumophila* in clinical samples obtained from Iranian patients. To this end, we conducted a systematic review and meta-analysis of studies conducted in different areas of the country. Studies published on the prevalence of *L. pneumophila* in clinical samples obtained from Iranian patients from January 2000 to July 2016 were included in our review. The overall prevalence of *L. pneumophila* was 9.6% (95% Cl: 8.2–11.1). The prevalence varied from 0.4% to 22.1% in different reports. This finding is inconsistent with other studies from different regions of the world [10–12].

Such inconsistencies may partly be related to the variations in climate conditions, exposition to contaminating sources (such as water), the penetrance of *Legionella* in the normal population [13], smoking frequency, the co-presence of other infectious diseases (such as chronic respiratory disease or other underlying chronic conditions), and finally the immune system competency [14].

Our results revealed that PCR-based methods were the most common molecular techniques used for detecting *L. pneumophila* in Iranian patients. Besides that PCR-based techniques are fast diagnostic approaches, these methods have unique features such as high sensitivity to detect even dead bacteria which are undetectable by culture-based methods, as well as the ability to detect a single organism by DNA amplification [15].

Subgroup analysis considering the time of the studies revealed that the prevalence of *L. pneumonia* was higher in the years 2009–2016 compared to 2000–2008 with frequencies of 9.2% (95% CI: 7.7–11.0) and 0.7% (95% CI: 8.0–14.3), respectively. This observation may partly be due to the development of diagnostic techniques with higher sensitivities in the recent years. Furthermore, and regarding the important role of this bacterium in pneumonia, extensive epidemiological studies have been conducted on this agent in the recent decade.

Subgroup analysis based on the location of the studies showed that the highest prevalence of *L. pneumophila* was observed in Ahvaz city. This observation can be related to the specific climate condition in this city that follows a biphasic pattern. In this biphasic pattern, the climate is much warmer during the first six months of the year compared to the second six months. This necessitates using air conditioners to cool the ambient temperature which exposes the people to *L. pneumophila* transmitted through these systems [16].

Interestingly, only the *L. pneumophila* serotype 1 was reported by all of the evaluated studies. In fact, molecular techniques have now provided sensitive methods to detect *L. pneumophila* serotype 1 in the context of Legionnaires' disease. Accordingly, most of the evaluated studies were carried out for detecting this serotype [17].

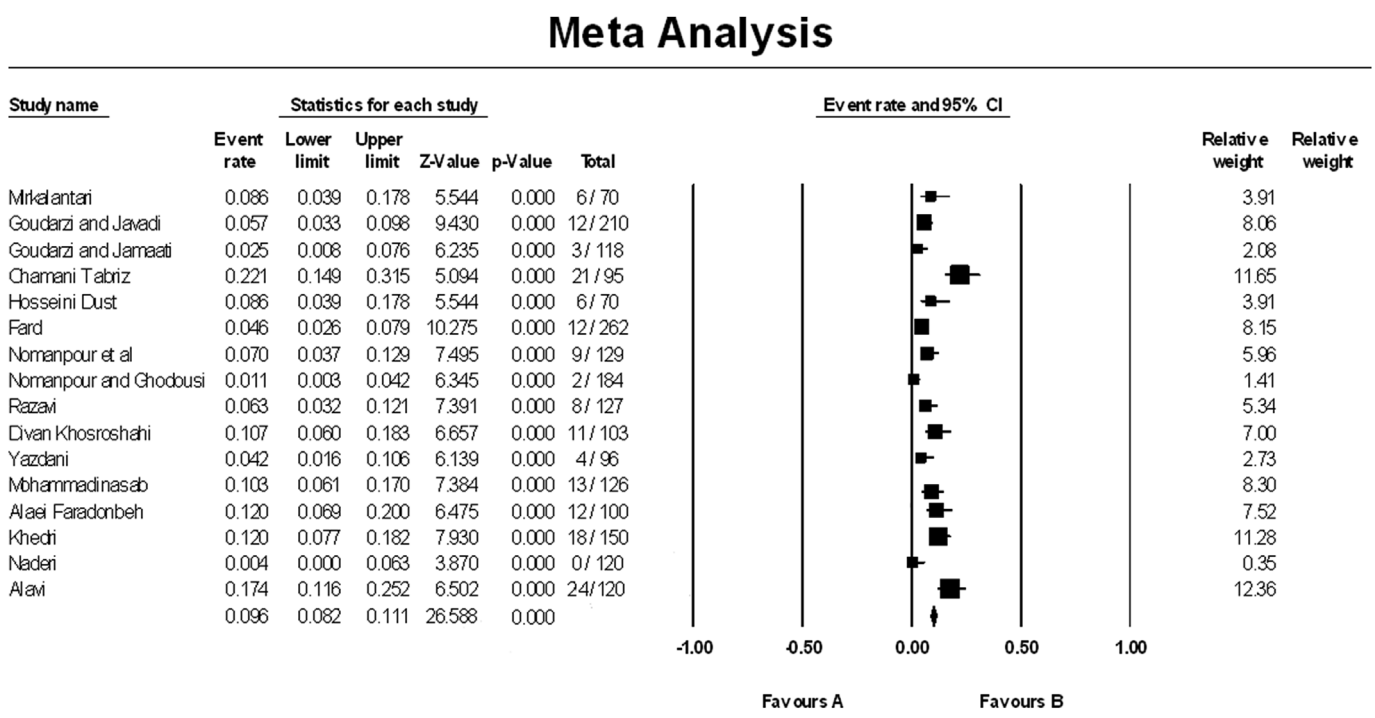

Fig. 2. Forest plot of the meta-analysis for the prevalence of *L. pneumophila* in Iranian clinical samples.

As a limitations of this study, the prevalence of *L. pneumophila* obtained here may not be generalizable to the whole country as this was based on the data recruited from some regions sparing other areas for which we found no reports.

5. Conclusion

The overall prevalence of *L. pneumophila* was 9.6% (95% Cl: 8.2–11.1), ranging from 0.4% to 22.1% in different studies. *L.*

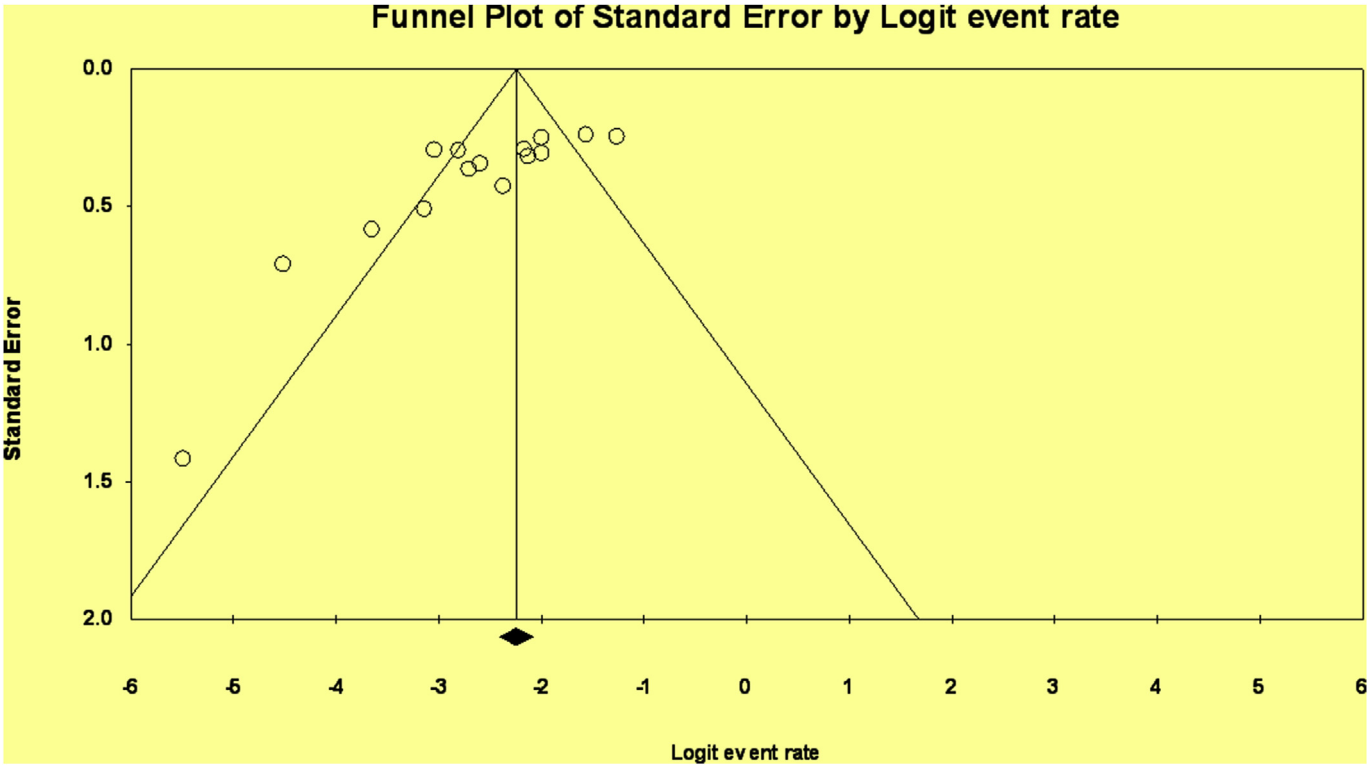

Fig. 3. Funnel plot for meta-analysis of the prevalence of *L. pneumophila* in Iranian clinical samples.

Table 1
Characteristics of enrolled studies for meta-analysis.

Prevalence Of Legionella (%)	Age (years)	event	Sample size	Location	Publication (years)	Time of study	study
8.5	35–80	6	70	Tehran	2008	–	Mirkalantari [18]
5.7	0.5–14	12	210	Tehran	2011	2010	Goudarzi and Javadi [19]
2.5	68.5	3	118	Tehran	2007	2004–2005	Goudarzi and Jamaati [20]
22.1	15–41	21	95	Tehran	2007	2006	Chamani Tabriz [21]
8.5	40–65	6	70	Tehran	2009	2007	Hosseini Dust [22]
4.6	–	12	262	Tehran	2012	–	Fard [23]
6.9	–	9	129	Tehran	2012	–	Nomanpour et al. [24]
1.08	4–69	2	184	Tehran	2011	–	Nomanpour and Ghodousi [25]
6.3	47.9	8	127	Tehran	2007	2004–2005	Razavi [26]
10.67	–	11	103	Qazvin	2015	–	Divan Khosroshahi [27]
4.16	–	4	96	Isfahan	2007	2002	Yazdani [28]
10.3	44	13	126	Yasuj	2013	–	Mohammadinasab [29]
12	48.4	12	100	Charmahal-O-Bakhtiri	2015	2012–2013	Alaei Faradonbeh [30]
12	–	18	150	Shahrekord	2015	2013	Khedri [31]
0	50.4 ± 22.6	0	120	Mashhad	2015	2013–2014	Naderi [32]
17.3	56	21	121	Ahvaz	2009	2007–2008	Alavi [14]

Table 2
Subgroups analysis for prevalence of *L. pneumophila* of clinical samples.

Sub-groups	No of studies	Heterogeneity test				Random model Egger's test			
		Z	*P*	Q	prevalence (95% Cl [%]	*p*	I^2	t	*P*
Over effect	16	26.5	0.00	63.4	9.6(8.2, 11.1)	0.00	76.3	4.1	0.00
Based on time of study (year)									
2000–2008	5	12.7	0.00	25.7	0.7(8.0, 14.3)	0.013	84.45	3	0.00
2009–2016	11	23.3	0.00	37	9.2(7.7, 11.0)	0.014	72.9	3	0.00
Based on sample size									
100 >	11	23.6	0.00	41.7	8.4(7.0, 10.1)	0.004	76	3.7	0.00
100≤	5	12.3	0.00	15	12.9(9.9, 16.7)	0.006	73.4	6.3	0.005
Based on location									
Tehran	9	20.7	0.00	41.8	7.8(6.3, 9.7)	0.047	80.8	2.3	0.00
Shahrekord	2	10.2	0.00	0.00	12.0(8.5, 16.6)	–	0.00	–	1.00
Qazvin	1	6.6	0.00	0.00	10.7(6.0, 18.3)	–	0.00	–	1.00
Isfahan	1	6.1	0.00	0.00	4.2(1.6, 10.6)	–	0.00	–	1.00
Yasuj	1	7.3	0.00	0.00	10.3(6.3, 17.0)	–	0.00	–	1.00
Mashhad	1	3.8	0.00	0.00	0.4(6.3, 17.0)	–	0.00	–	1.00
Ahvaz	1	6.5	0.00	0.00	17.4(11.6, 25.2)	–	0.00	–	1.00

pneumophila is a major cause of community- and hospital-acquired pneumonia. It is of pivotal importance to recruit sensitive and reliable molecular and culture-based techniques to detect and control this infection in healthcare environments.

Acknowledgment

We would like to thank our colleagues for their help in this study.

List of abbreviations

CAP	Community-Acquired Pneumonia
HAP	Hospital Acquired Pneumonia
BCYE	Buffered Charcoal Yeast Extract
PCR	Polymerase Chain Reaction
DFA	Direct Fluorescent Antibody
ELISA	The Enzyme-Linked Immunosorbent Assay
COPD	Chronic Obstructive Pulmonary Disease
BAL	Bronchoalveolar Lavage
CI	Confidence Interval

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

[1] H. Friedman, Y. Yamamoto, T.W. Klein, Legionella pneumophila Pathogenesis and

Immunity. Seminars in Pediatric Infectious Diseases, Elsevier, 2002, pp. 273–279.
[2] P.H. Edelstein, R.D. Meyer, S.M. Finegold, Laboratory diagnosis of Legionnaires' disease 1–4, Am. Rev. Respir. Dis. 121 (1980) 317–327.
[3] A. Khaledi, A. Bahrami, E. Nabizadeh, Y. Amini, D. Esmaeili, Prevalence of Legionella species in water resources of Iran: a systematic review and meta-analysis, Iran. J. Med. Sci. 43 (2018) 571.
[4] E. Leoni, P. Legnani, Comparison of selective procedures for isolation and enumeration of Legionella species from hot water systems, J. Appl. Microbiol. 90 (2001) 27–33.
[5] B.D. KIRBY, K.M. SNYDER, R.D. MEYER, S.M. FINEGOLD, Legionnaires' disease: report of sixty-five nosocomially acquired cases and review of the literature, Medicine 59 (1980) 183–205.
[6] M. Sabria, L.Y. Victor, Hospital-acquired legionellosis: solutions for a preventable infection, Lancet Infect. Dis. 2 (2002) 368–373.
[7] A. Granados, D. Podzamczer, F. Gudiol, F. Manresa, Pneumonia due to Legionella pneumophila and pneumococcal pneumonia: similarities and differences on presentation, Eur. Respir. J. 2 (1989) 130–134.
[8] N. Sopena, M. Sabria-Leal, M.L. Pedro-Botet, E. Padilla, J. Dominguez, J. Morera, et al., Comparative study of the clinical presentation of Legionella pneumonia and other community-acquired pneumonias, Chest. J. 113 (1998) 1195–1200.
[9] Evans GE. Development of Legionella Spp. Specific Primers Which Eliminate Interference by Contaminating DNA in Qiagen Extraction Columns.
[10] Y.-F. Ngeow, S. Suwanjutha, T. Chantarojanasriri, F. Wang, M. Saniel, M. Alejandria, et al., An Asian study on the prevalence of atypical respiratory pathogens in community-acquired pneumonia, Int. J. Infect. Dis. 9 (2005) 144–153.
[11] N. Behbehani, A. Mahmood, E. Mokaddas, Z. Bittar, B. Jayakrishnan, M. Khadadah, et al., Significance of atypical pathogens among community-acquired pneumonia adult patients admitted to hospital in Kuwait, Med. Princ. Pract. 14 (2005) 235–240.
[12] M.T. Montagna, C. Napoli, D. Tatò, G. Spilotros, G. Barbuti, S. Barbuti, Clinical–environmental surveillance of legionellosis: an experience in Southern Italy, Eur. J. Epidemiol. 21 (2006) 325–331.
[13] H.K. Lee, M.K. Woo, Y.I. Ju, S.J. Baek, H.J. Song, J.S. Choi, et al., Prevalence of antibodies in response to Legionella species, analysis of a healthy population from Jeollanam-do Province, Korea, J. Microbiol. 46 (2008) 160–164.
[14] S.M. Alavi, N. Moshiri, M. Moosavian, F. Yusefi, E. Abbasi, Seroprevalence of Legionella Pneumophila in admitted patients with pneumonia in training hospitals, Ahvaz, Iran, J. Med. Sci. (2009) 811–816.
[15] D.H. Persing, D.H. Persing, Diagnostic Molecular Microbiology: Principles and Applications, (1993).
[16] B. Todd, Legionella Pneumonia: many cases of Legionnaire disease go unreported or unrecognized, AJN Am. J. Nurs. 105 (2005) 35–38.
[17] T. Shimada, Y. Noguchi, J.L. Jackson, J. Miyashita, Y. Hayashino, T. Kamiya, et al., Systematic review and metaanalysis: urinary antigen tests for Legionellosis, CHEST Journal 136 (2009) 1576–1585.
[18] S. Mirkalantari, A. Mohabati Mobarez, S.R. Hoseini Dost, J. Aslani, Isolation of Legionella from BAL samples of Legionella pneumonia patients, by PCR and Culture Methods, Modares J. Med. Sci. Pathobiol 10 (2008) 75–83.
[19] H. Goudarzi, S. SeyedJavadi, M. Goudarzi, Detection of Legionella pneumophila by Sputum Culture, Direct Immunoflurscence and PCR, (2011).
[20] H. Goudarzi, H.-R. Jamaati, G. Eslami, F. Fallah, R. Khanipourroshan, Urinary antigen test EIA: a valuable rapid clinical method for the diagnosis of legionella, Arch. Clin. Infect. Dis. 2 (2007).
[21] L.C. Tabriz, M. Jeddi-Tehrani, S. Motahari, H. Zeraati, S. Asgari, M. Karegar, et al., Detection of Legionella pneumophila by nested PCR-RFLP and ELISA on urine specimens of pregnant women with respiratory infections, J. Reproduction Infertil. 8 (2007).
[22] R. Doust, A. Mobares, S. Mirkalantar, J. Aslani, A. Fuladi, Nosocomial Legionnaires' disease outbreak in tehran, Res. J. Microbiol. 4 (2009) 23–30.
[23] S. Fard, B. Nomanpour, B. Fatolahzadeh, A. Mobarez, D. Darban-Sarokhalil, A. Fooladi, et al., Hospital acquired pneumonia: comparison of culture and real-time PCR assays for detection of Legionella pneumophila from respiratory specimens at Tehran hospitals, Acta Microbiol. Immunol. Hung. 59 (2012) 355–365.
[24] B. Nomanpour, A. Ghodousi, T. Babaei, S. Jafari, M. Feizabadi, Single tube real time PCR for detection of Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydophila pneumoniae and Legionella pneumophila from clinical samples of CAP, Acta Microbiol. Immunol. Hung. 59 (2012) 171–184.
[25] B. Nomanpour, A. Ghodousi, T. Babaei, S. Mousavi, S. Asadi, M. Feizabadi, Detection and quantification of Streptococcus pneumoniae from Iranian patients with pneumonia and individual carriers by real time PCR, Afr. J. Biotechnol. 10 (2011) 12826–12832.
[26] S.M. Razavi, H. Ziaee, T. Mokhtari-Azad, H. Rasoul, T. Doroodi, A. Mirsalehian, et al., Surveying respiratory infections among Iranian Hajj pilgrims, Archives of Clinical Infectious Diseases 2 (2007).
[27] N.D. Khosroshahi, T.N. Farivar, P. Johari, Identification of Legionella pneumophila in intubated patients with TaqMan real time PCR, Jundishapur J. Microbiol. 8 (2015).
[28] R. Yazdani, Diagnosis of Legionella pneumophila by direct fluorescent Antibody (dfa) technique in bronchoalveolar specimens of pneumonia patients referring to medical centers in isfahan, 2002, SSU. J. 14 (2007) 64–68.
[29] M. Mohammadinasab, A. Khosravani, F. Kafilzade, A. Jahangirisisakht, R. Mohammadi, R. Abasi, Prevalence of bordetella pertussis, and Legionella pneumophila in patients with pneumonia diagnosis in shahid beheshti hospital by culture and multiplex PCR, Armaghane danesh 18 (2013) 622–631.
[30] F.A. Faradonbeh, F. Khedri, A. Doosti, Legionella pneumophila in bronchoalveolar lavage samples of patients suffering from severe respiratory infections: role of age, sex and history of smoking in the prevalence of bacterium, Srp. Arh. Celok. Lek. 143 (2015) 274–278.
[31] F. Khedri, F.A. Faradonbeh, M. Eliyasi, A. Barghi, A. Doosti, P. Emad, et al., Molecular depiction of lepa, lida, ralf, rtxa and ivhb virulence factors of legionella pneumophila isolated from respiratory tract infections, Int. Arch. Med. 8 (2015).
[32] H. Naderi, F. Sheybani, M. Sarvghad, Z. Meshkat, M.J. Nooghabi, Etiological diagnosis of community-acquired pneumonia in adult patients: a prospective hospital-based study in mashhad, Iran, Jundishapur J. Microbiol. 8 (2015).